Recommendations of Select Subcommittee to develop Mefloquine Study Options

AFEB May 12, 2004

Background

Research Questions:

1. What are the comparative rates of adverse events (Including neuropsychiatric) among deployed service members using mefloquine versus doxycycline or no antimalarial medication?
2. What are the attributable risk factors (including mefloquine) for suicide among deployed and recently deployed service members?

Discussions

The Subcommittee reviewed:

- Historical experience with malaria
- Pertinent data sources (personnel, health encounter, post-deployment health, serum repository)
- Pharmacy data and clinical practices
- DoD mortality surveillance
- DoD suicide surveillance
- The Millennium Cohort Study
- Medical Literature on anti-malarials

RECOMMENDATIONS

Careful and well-constructed descriptive studies of the outcomes potentially related to mefloquine is a prerequisite to any subsequent studies.

RECOMMENDATIONS

To assess adverse events associated with mefloquine, the Board recommends either a retrospective, cross-sectional, or prospective cohort study approach.

RECOMMENDATIONS

Because of the rare nature of suicide and the large number of variables that need to be assessed, the Board feels a case-control study design is the most appropriate for studying factors associated with suicide, including mefloquine.

RECOMMENDATIONS

Other Recommendations:

- Millennium Cohort
- Serum Repository
- Coordinate with VA
- Transparency
  - Non-DoD investigator collaboration with DoD
  - Non-DoD oversight
- Consider compliance

Discussion/Questions

Force Health Protection and Readiness

Recommendations

1. Document mefloquine use better
2. Descriptive studies first to identify potential associations for analysis
3. Use serum repository for objective documentation of mefloquine use
4. Consider Millennium Cohort
5. Comprehensive review of DoD suicides

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6. For suicide: Case-control study design
7. For adverse events associated with mefloquine: Cross-sectional, retrospective study design or a prospective cohort study
8. For more common, less severe adverse events: Randomized double-blind study
9. Compliment knowledge/attitudes/beliefs study with compliance study

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10. Consider studies of individual characteristics among those who experience severe adverse events
    - Including biological and genetic markers
11. Coordinate Dept of Veterans Affairs
12. Ensure transparency of work
13. Independent non-DoD oversight committee

Significant Issues

The Subcommittee noted challenges in:

- Quality issues for data from deployed settings
  - Especially for in-theater Rx
- Lack of compliance data for anti-malarial use
  - leading to misclassification bias
- Obtaining reliable denominator information
- General difficulty of doing research studies in operational military settings
- Studying Suicide objectively
  - Case definitions, multifactorial origin, confounders